Remarks

The Examiner has objected to, but entered, the Preliminary Amendment[1] alleging that said amendment contains new matter. *See*, Paper No. 9, page 2, item 1 and page 3, item 4, last sentences bridging to top of page 4. In particular it was alleged that, "The artisan reading the 09/062815 application would have no idea that the recited 'NT74' was meant to read 'NTT4'". *See*, Paper No. 9, page 4, first full sentence. Therefore, the Examiner indicated that the present application is a Continuation-In-Part application instead of a Divisional. *See*, Paper No. 9, page 4, first paragraph, last sentence.

Applicants respectfully disagree that the Preliminary Amendment introduces new matter by amending a simple clerical error wherein a "7" was substituted for a "T" in the acronym "NTT4". However, Applicants assert that the present application is a Divisional application, not a Continuation-In-Part. Therefore, Applicants have herein amended "NTT4" to recite "NT74" as originally filed in the specifications of the parent applications to which this application claims priority.

Claims 1, 14, 17-20, 22 and 23 have been canceled herein without prejudice or disclaimer. Claims 2-13, 15, 21, 24-29 were previously canceled. Applicants reserve the right to pursue the subject matter of all canceled claims in one or more divisional or continuation applications. Claims 16 and 30 have been amended pursuant to suggestions or remarks made by the Examiner (discussed below). Support for amended claims 16 and 30 can be found in the specification as filed. For example, support can be found at page 21, third paragraph to page 22, first paragraph (antibodies generated against polypeptides of the invention). Claims 47-51 have been added to encompass subject matter previously in the Markush groups of claims 44 and 46. Thus, claims 44 and 46 have also been amended to delete reference to the subject matter now encompassed by claims 47-51. Support for new claims 47-51 can be found in the specification as filed; for example, at page 21, fourth paragraph (human antibodies) and at page 21, second paragraph (monoclonal and polyclonal antibodies). Upon entry of the present amendment, claims 16 and 30-51 will be pending. No new matter has been added by these amendments.

[1] Submitted with the present application when it was filed on August 8, 2001

Objection to the Drawings

The Examiner has objected to the drawings, and requested correction thereof, because "there does not appear to be a Figure 1E that could be matched to the new Figure 1D." *See*, Paper No. 9, page 4, item 5. Applicants submit that no correction is necessary because the Examiner has simply mistaken the informal drawings for the formal drawings. Applicants note that when present application was filed, four (4) sheets of Formal Drawings were submitted along with five (5) sheets of informal drawings. *See enclosed*, copy of return receipt postcard date stamped 08/08/01, item #2 ("5 sheets drawings") and item #6 ("4 Sheets of Formal Drawings"). For the Examiner's convenience Applicants enclose herewith a copy of the five sheets of informal drawings (Fig. 1A-1E) which are arranged in landscape format (*i.e.*, figure is viewed with the long edge of the paper horizontal), and also a copy of the four sheets of Formal Drawings (Fig. 1A-1D) arranged in portrait format (long edge of the paper vertical). Only the latter set of Formal Drawings should be published when the present application becomes an issued patent. In sum, Applicants submit that a correction of drawings is unnecessary because the originally submitted Formal Drawings correctly comprise only sheets 1A-1D.

Rejection of Claims 14 and 16

Claim 14 was rejected under 35 U.S.C. § 112, second paragraph, based on inclusion of the terms "analogs" and "derivatives". *See*, Paper No. 9, page 5, last paragraph of item 7. Claim 14 was also withdrawn from consideration as being drawn to a nonelected invention. *See*, Paper No. 9, page 2, item 3. Applicants have herein canceled claim 14 thereby rendering the rejection of this claim moot.

Claim 16 was rejected under 35 U.S.C. § 112, second paragraph. The Examiner suggested this claim be amended to recite "an antibody raised against the polypeptide of claim 14". *See*, Paper No. 9, page 5, item 7. Applicants have herein amended claim 16 in accordance with the Examiner's suggestion, except that Applicants have used the phrase "generated against" instead of "raised against"; the former phrase having more explicit support in the specification as filed. *See e.g.*, specification at page 21, third paragraph (describing "Antibodies generated against the polypeptides..."). Additionally, claim 16 has been rewritten into independent form

by incorporating the description of the polypeptides previously in claim 14. This additional amendment was necessary in view of the withdrawal of claim 14 from consideration and the cancellation of claim 14 subsequently made herein. Applicants also note that amended claim 16 does not include the terms "analogs" or "derivatives" previously objected to by the Examiner in claim 14. No new matter has been added by the amendment of claim 16. In view of the amendment of claim 16, Applicants respectfully request that the rejection under 35 U.S.C. § 112 be reconsidered and withdrawn.

Rejections under 35 U.S.C. § 101

Claims 16 and 30-46 were rejected under 35 U.S.C. § 101 based on an allegation that "the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility." *See*, Paper No. 9, page 5, item 8. Moreover, although it was initially recognized that the pending claims are directed to *antibodies,* the majority of the rejection focused on the utility of NTT polypeptides and nucleic acids. *Compare*, Paper No. 9, sentence bridging the bottom of page 5 to top of page 6 *with* Paper No. 9, second paragraph on page 6 through penultimate paragraph on page 8.

Applicants respectfully disagree and traverse the rejection. For the record, Applicants submit that the specification does, in fact, disclose specific and substantial utilities for NTT polypeptides and nucleic acids. However, Applicants also point out that the presently claimed invention is not polypeptides or polynucleotides, but rather *antibodies* that bind NTT polypeptides. Moreover, even *if* it were true that the specification failed to disclose specific and substantial utilities for NTT polypeptides and polynucleotides, it does not follow that the claimed antibodies would also lack specific and substantial utility. In particular the claimed antibodies, *at the very least*, constitute research reagents. And, it has long been acknowledged and accepted that research reagents comprise patentable subject matter[2] meeting the utility requirement of 35 U.S.C. § 101. Therefore, at a minimum, the presently claimed antibodies have patentable utility

[2] As a small sampling of examples in this regard, Applicants submit herewith copies five granted U.S. patents that claim research reagents. *See*, U.S. Patent Nos. 6,531,301 "Nucleic Acid-Free Thermostable Enzymes And Methods of Production Thereof"; 5,741,646 "Cell Lines And Methods For Screening Growth Regulatory Compounds"; 5,391,487 "Restriction Endonuclease SGFI From *Steptomyces Griseoruber*"; 4,543,439 "Production And Use of Monoclonal Antibodies To Phosphotyrosine-Containing Proteins"; and, 4,529,700 "Hybridoma Cells Secreting A Monoclonal Antibody Specific For 5-Bromo And 5-Iodoeoxyuridine And Reagents For Measuring Cellular Proliferation".

as research reagents. For example, in addition to the teachings provided in the present specification[3], those of ordinary skill in the art would recognize that antibodies that bind NTT would also be useful for even further characterizing NTT tissue specific expression patterns or biological activities. As one particular example, NTT antibodies are useful for characterization of the temporal and tissue specific expression patterns of NTT during embryogenesis. Hence, Applicants submit that the presently claimed antibodies have, *at the very least*, well established utility as research tools.

Furthermore, Applicants point out and emphasize that the claimed antibodies do not "merely define a starting point for further research" (*see*, Paper No. 9, page 7) because the antibodies are not the objects of research. Instead, the claimed antibodies are useful as tools in research. Stated another way, the claimed antibodies are not the *objects* upon which further experimentation would be performed, but are instead the objects which can be used to perform experimentation. And, since Applicants are not currently claiming the object to which the claimed antibodies bind (*i.e.,* NTT polypeptides), the utility of NTT polypeptides is not relevant to the present inquiry. NTT antibodies can, and do, have utility independent of the utility of NTT polypeptides. Thus, in view of the above explanation and clarification, Applicants respectfully request that the rejection of claims 16 and 30-46 under 35 U.S.C. § 101 be reconsidered and withdrawn.

Rejection of claims 16 and 30-46 under 35 U.S.C. § 112, first paragraph

Claims 16 and 30-46 were rejected under 35 U.S.C. § 112, first paragraph, based upon a premise that "since the claimed invention is not supported by either a specific and substantial, asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention so that it would operate as intended without undue experimentation." *See*, Paper No. 9, page 8, item 9.

Applicants respectfully disagree and traverse. In particular, Applicants respectfully submit that, as explained in the present response (see above), claims 16 and 30-46 are supported by specific, substantial, and/or well established utilities. Hence, in view of the present

[3] The specification teaches, for example, that the NTT cDNA was cloned from a fetal brain (see, page 4, fourth paragraph) and that NTT message is abundantly expressed in human brain (see, page 27, example 3).

application's original disclosure and the high level of skill and knowledge in the antibody arts[4], Applicants submit that one of ordinary skill in the art would certainly know how to use the claimed antibodies.

Claim 16 was also rejected under 35 U.S.C. § 112, first paragraph, because it "encompasses antibodies that bind...'analogs' and 'derivatives' of the polypeptide of SEQ ID NO:2..." *See*, Paper No. 9, page 9, first paragraph to page 11, first paragraph; and, page 11, item 10. Applicants note that the above rejection is now moot in view of the amendment made herein which has eliminated reference to "analogs" and "derivatives" from claim 16.

Claims 34 and 45 were also rejected under 35 U.S.C. § 112, first paragraph, on the alleged basis that, "claims 34 and 45 require human antibodies to the human protein SEQ ID NO:2...there is no disclosure of such, and nor are such known in the art." *See*, Paper No. 9, page 12, second paragraph (emphasis added). Applicants respectfully disagree and traverse.

First, Applicants assume the Examiner intended the above rejection to be drawn to claim 46 instead of claim 45, since claim 45 is not limited to human antibodies but claim 46 does encompass human antibodies. Applicants response is based on this presumption. If such a presumption is not correct, Applicants request further clarification of the rejection of claim 45. Second, it is correct that human NTT antibodies were not known in the art when the present application was filed (thus establishing novelty of the present invention). However, it is not correct that human antibodies or methods for producing human antibodies were not known in the art as of May 16, 1994 (*i.e.*, the earliest claimed priority date in the present application). For example, Applicants enclose herewith copies of five different pre-filing date publications which describe methods for making human antibodies (see enclosed Exhibits A, B, C, D, and E). Furthermore, the specification as originally filed also provided specific examples of methods for making human antibodies, for example, at page 21, last full paragraph. Accordingly, Applicants respectfully request the rejection of claims 16 and 30-46 under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

[4] See e.g., Harlow and Lane, "Antibodies a Laboratory Manual", 2nd Edition, Cold Spring Harbor Laboratory (1988). See also, *In Re Wands*, 858 F.2d 731, 740 (Fed. Cir. 1988) ("There was a high level of skill in the [antibody] art at the time when the application was filed [in], and all of the methods needed to practice the invention were well known.").

Rejection of claims 16 and 30-33, 36-39, 45 and 46 under 35 U.S.C. § 102(b)

Claims 16 and 30-33, 36-39, 45 and 46 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Wadzinski, *et. al.* (J. Biol. Chem. 267(24)16883-16888 (1992)) which discloses an anti-HA antibody. In particular, the rejection was based on the premise that:

> The claims require an antibody that binds a polypeptide that *comprises* the sequence of SEQ ID NO:2. Thus, the polypeptides of the claims encompass proteins that have amino acid sequences *in addition* to that of SEQ ID NO:2, e.g. carrier or tag sequences, and the claimed antibodies need only bind to those additional sequence and not to amino acids encompassed by SEQ ID NO:2.

See, Paper No. 9, page 13, item 12 (emphasis in original).

Applicants respectfully disagree. Currently amended claim 16 does not recite "comprises", therefore, the present rejection is inapplicable to this claim. Applicants have herein amended claim 30 (and thereby dependent claims 31-33 and 36-39) to more explicitly indicate that the claimed antibodies bind to the polypeptide of the invention. And, Applicants respectfully submit that the language of claim 45 (and thereby dependent claim 46) already clearly indicates that the claimed antibodies *bind to polypeptides of the present invention*. In view of the above explanations and amendment, Applicants respectfully request that the rejection of claims 16 and 30-33, 36-39, 45 and 46 under 35 U.S.C. § 102(b) be reconsidered and withdrawn.

Conclusion

Applicants respectfully request that the above-made amendments and remarks be entered and made of record in the file history of the instant application. The Examiner is invited to call the undersigned at the phone number provided below if any further action by Applicant would expedite the examination of this application.

If there are any fees due in connection with the filing of this paper, please charge the fees to our Deposit Account No. 08-3425. If a fee is required for an extension of time under 37 C.F.R. § 1.136, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,

Date: 9/12/2003

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